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Filed : December 7, 2001

REMARKS

The specification has been amended as set forth above to list the application number for U.S. Provisional Application No. 60/337,017 (the '017 application). The serial number for the '017 application previously was not listed because that application was filed on the same date as the parent application for the instant application. Thus, the provisional application number was not available as of the filing date of the instant application. It is worth noting that the title and filing date for the provisional application were listed in the instant specification as filed. Thus, no new matter is added by the amendment to the specification.

No amendments have been made to the claims in this response. Claims 1-5, 29-37 and 38-57 are pending in the application, with Claims 1 and 42 being the only independent claims.

Discussion of Rejection under 35 U.S.C. § 112, Written Description

The Examiner rejected Claims 1-5 and 29-36 and 38-57 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. According to the Examiner, the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the Examiner argues that the "instant specification ... has described only several housekeeping epitopes from seven cancer-related proteins." The Examiner argues that "[t]he specification fails to describe any structural properties that are shared between housekeeping epitopes, only that they are processed by standard proteasomes, not immunoproteasomes." Furthermore, the Examiner asserts that "there is no disclosure of the enzymes, cofactors and/or chaperonins responsible for the differential processing of housekeeping epitopes."

The Examiner also argues that "T cells which recognize 'housekeeping' epitopes may also recognize 'immuno'-epitopes" and that "there is no disclosure in the specification on how to distinguish the T cells of the claimed composition from other T cells other than the fact that they are able to bind to epitopes produced by standard proteasomes that are not produced by immunoproteasomes." The Examiner continues that "[b]ecause there is no disclosure of any actual structural difference between housekeeping and immune epitopes, there is no reason to believe that a T cell which binds to a discovered housekeeping epitope cannot also bind an immuno-epitope with a related set of anchor residues." The Examiner cites *Fiers v. Revel* (25 U.S.P.Q.2d 1016 (1993)) for the

proposition that adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it.

In order to satisfy the written description requirement, a patent application must describe the invention in sufficient detail that one of skill in the relevant art could conclude that the inventor was in possession of the claimed invention at the time the application was filed. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991). Compliance with the written description requirement of 35 U.S.C. § 112 is essentially a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed. *See id.* at 1563 (citing *In re DiLeone*, 436 F.2d 1404, 1405, 168 U.S.P.Q. 592, 593 (CCPA 1971)). A functional description of a material can be sufficient for the written description requirement. *See Enzo Biochem, Inc. v. Gen-Probe Incorporated*, 296 F.3d 1316, 1324 (Fed. Cir. 2002). The Federal Circuit has adopted the standard that "the written description requirement can be met 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, *functional characteristics when coupled with a known or disclosed correlation between function and structure*, or some combination of such characteristics.'" *Id.* (quoting from the Written Description Guidelines, 66 Fed. Reg. at 1106).

Respectfully, here the written description requirement has been satisfied for the claimed subject matter because the specification fully described the claimed subject matter as of the filing of the application. In particular, the written description requirement has been satisfied for housekeeping epitopes because the specification provides sufficiently detailed, relevant identifying characteristics including partial structure for all housekeeping epitopes, other physical and/or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, and complete sequence structure for at least one working example.

The specification describes all of the relevant identifying characteristics for all housekeeping epitopes. In short, a housekeeping epitope is a polypeptide that: 1) is a protein fragment formed via activity of a housekeeping proteasome; 2) has a known or a predicted affinity for a class I MHC molecule; and 3) is displayed on the surface of cells in which the housekeeping proteasome is predominantly active. These features are discussed in more detail below.

As stated above, one feature that housekeeping epitopes all share is that they are polypeptide fragments of larger proteins and are formed via activity of the housekeeping proteasome that is predominantly active only in certain cell types under certain conditions. Specifically, the housekeeping proteasome is predominantly active in peripheral cells, including neoplastic or chronically infected cells, so long as such peripheral cells are not undergoing interferon-induced gene expression. Housekeeping proteasomes are not predominantly active in pAPCs. The C-terminus of a housekeeping epitope will correspond to the C-terminus of a fragment produced by the action of a housekeeping proteasome. Also, another feature that housekeeping epitopes all share is that each has an affinity for at least one allele product of class I major histocompatibility complex (MHC). Further, another feature that housekeeping epitopes all share is that they are displayed on the surface of cells in which the housekeeping proteasome is predominantly active. The specification provides all of the above-mentioned relevant identifying characteristics for all housekeeping epitopes, which include the partial structure and properties for all housekeeping epitopes, including all of the housekeeping epitopes in the application. *See for example*, page 110, lines 1-11; page 22, lines 16-26; page 20. line 29 to page 21, line 1; page 110, line 32- page 111, line 2; and page 41, lines 11-24.

Further, there is a disclosed correlation between the structure of the housekeeping epitopes and their function, for example being epitopes that are displayed on a cell in which a housekeeping proteasome is predominantly active. Display on a target cell is dependent upon MHC binding and presentation. MHC I binding capability correlates with the sequence structure of the epitope. The specification explains that the encoded MHC epitopes are preferably 9-10 amino acids in length, and numerous MHC alleles are known in the art and disclosed in the written description. *See Specification* at page 110, lines 1-2. The housekeeping epitopes are disclosed as having the preferred size for MHC binding and as having amino acid motifs with affinity for class I MHC. Thus, the common features are highly correlated with structure. For housekeeping epitopes, function is dependent upon structure, and function is a proxy for the underlying structure from which they are so specifically formed from an antigenic protein. Therefore, the specification discloses a correlation between the function and structure of housekeeping epitopes.

As noted in the Office Action, the specification describes various housekeeping epitopes. One example is a housekeeping epitope from tyrosinase, FLPWHRLFLL. This working example from Tyrosinase is representative of all housekeeping epitopes. The housekeeping epitope is representative in terms of its length of 10 amino acids, its region having MHC binding affinity, its having a proper C-

terminus, for example, one that is produced through processing by the housekeeping proteasome. Applicants respectfully assert that the disclosure of general common features of this genus, together with the above-mentioned epitope that exemplifies the common features of the claimed genus, is sufficient to satisfy the written description requirement under the *Written Description Guidelines*.

Applicants also note that the instant specification at page 137, lines 3-6, incorporates by reference the entirety of U.S. Provisional Application Nos. 60/282,211 and 60/337,017 filed on April 6, 2001 and November 7, 2001, respectively, which applications include numerous additional housekeeping epitope species. However, the unifying characteristics of this genus, having been fully disclosed in the original priority applications, are not any further elucidated by reference to the numerous examples in the provisional applications. This fact stands as evidence that description of the basic characteristics in the original priority applications was adequate to describe the genus. There simply is no better way of describing the genus, and there are no "missing" structural features that would only be discernable by reference to additional exemplary sequences.

Finally, Applicants respectfully assert that satisfaction of the written description requirement does not depend upon whether a T cell may recognize a housekeeping epitope and an immune epitope with similar anchor residues in the context of an MHC complex. Cross-reactivity does not bear on written description. Furthermore, it would be the similarity of the non-anchor residues that would have the greater impact on cross-reactivity. As for the assertion in the Office Action that there is no disclosure of the enzymes, cofactors and/or chaperonins responsible for the differential processing of housekeeping epitopes, Applicants respectfully disagree. The proteasomes and their different subunits are fully described in the application. Applicants direct the Examiner's attention, for example, to the specification at page 23, line 15 to page 24, line 28 ("Different Proteasomes Yield Different Epitopes"); page 25, line 28 to page 26, line 4; and Figure 2.

As discussed above, the specification has fully described the genus of housekeeping epitopes in satisfaction of the written description requirements. The specification also describes isolated T cells, where each T cell expresses a T cell receptor specific for an MHC-peptide complex comprising a first housekeeping epitope. *See for example, specification* at pages 107-108. Furthermore, the specification describes how to test to verify that a given T cell expresses a T cell receptor specific for an MHC-peptide complex comprising a first housekeeping epitope, which permits one of skill in the art to distinguish members of the claimed genus. Therefore, one of skill in the art would recognize that applicants possessed the claimed subject matter at the time of filing the application.

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Thus, reconsideration and withdrawal of the instant rejection is respectfully requested.

Conclusion

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, arguments in support of the patentability of the pending claim set are presented above. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: 11/3/05

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